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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/582,842	07/05/00	SUGIYAMA K	060017

HM12/1004

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EXAMINER	
D.O.P	
ART UNIT	PAPER NUMBER
1641	3

DATE MAILED: 10/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/582,842	SUGIYAMA ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 July 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-6, 13, 14, 16, 17, 20, please use conventional claim language, e.g. comprising, having, including, etc. and avoid superfluous wordings such as "characterized in".

Claims 1-21 are indefinite as to what biotin-introduced products are, e.g. a biotinylated substance or just a biotin?

Claims 4-5 lack method steps.

The first step of claim 6 is unclear. Please recite step (1) in the active tense, e.g. combining a sample...with reagents...etc.

Claims 9 and 12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim 7. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9, 10, 12-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haughland et al. (US 5,443,986) further in view of Sano (US 6,022,951).

Haughland teaches a biotin-avidin-biotin complex comprising two biotin-introduced products which are the same or different (see table 12 in col. 22); and a cross-linked avidin sandwiched therebetween (see col. 22, table 12) wherein at least one of the two biotin-introduced products is labeled and the other one is a biotin-introduced binding component (see col. 12, col. 22). Haughland also teaches an enzyme-mediated technique such as enzyme-linked immunosorbent assay (ELISA) to detect analytes (see col. 22, lines 4-51). The binding component is a DNA (see col. 22, table 12). The biotin-introduced labeling substance is a biotin-introduced enzyme (see col. 22, table 12). Kits containing reagents for carrying out the methods are also disclosed in Haughland (see col. 40, example 19).

However, Haughland fails to teach a cross-linked avidin.

Sano teaches a crosslinked avidin or streptavidin having increased stability or increased affinity for binding biotin. The crosslinkers are disuccimidyl glutarate, dimethyladipimidate, bissulfo(succinimidyl)suberate, etc. Crosslinking can occur within and between subunits and domains. It has been determined that domain stability directly correlates with biotin binding. Streptavidin proteins with increased domain-domain stability also have an increased affinity for biotin (See col. 9, lines 45-60).

It would have been obvious to one of ordinary skill in the art to use the crosslinked streptavidin of Sano in the method of Haughland since the crosslinked streptavidin is more stable and has high biotin affinity than the non-crosslinked streptavidin and thus the complex of biotin-crosslinked avidin-biotin would be more stable. An increase in affinity and stability between the avidin/streptavidin and the biotin would be an advantage in reduced product storage. Assays and kits comprising increased affinity streptavidin/avidin, because of the additional stability, have a longer shelf and less fastidious in shipping and storage requirements. The enhanced stability of these assays and kits would reduce the cost to the consumer. (See col. 15, lines 35-55).

Claims 8, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haughland et al. (US 5,443,986) further in view of Tatsumi (US 5,843,746).

Haughland et al. Has been discussed above.

However, Haughland fails to teach a biotin-introduced fused-protein of an enzyme such as a biotin-introduced luciferase and a Fab' antibody fragment.

Tatsumi teaches a fusion protein (biotinated firely luciferase) which can be applied to a variety of bioluminescent analysis methods. For example, the biotinated firely luciferase can be bound through the biotin thereof to avidin or streptavidin to form a luciferase complex and a luminescent analysis method using such a firely luciferase complex can be applied to a detection system using biotin-avidin in techniques such as enzyme immunoassays, DNA probe method, immunostaining, receptor measurement, in situ hybridization, etc. (see col. 3, lines 33-41; col. 4, lines 25-35). Tatsumi also

teaches using goat anti-mouse IgG Fc fragment-specific polyclonal antibody in the method of detecting for the enzyme activity. (see col. 7, lines 40-55).

It would have been obvious to one of ordinary skill in the art to use the fused protein of Tatsumi in the method of Haughland for detecting the activity of luciferase since Haughland teaches an enzyme immunoassay method of using binding agent-biotin-avidin-biotin-enzyme and the enzyme luciferase of Tatsumi can be biotinylated. Since the biotinated firely luciferase of Tatsumi yields a much higher percentage of activity upon binding to streptavidin compared to that of a chemically modified biotinated firely luciferase, e.g. 93% to 62% respectively. Furthermore, the biotinated firely luciferase of Tatsumi attains 10 times sensitivity as high as the conventional chemically modified biotinated firely luciferase. With respect to the fragment Fab', since it depends on the analyte being detected, one of ordinary skill in the art would find it obvious to use fragment Fab's in the detection of antigen since fragment Fab' provides specificity

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 703-308-4398. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-746-5291 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Pensee T. Do
Patent Examiner
October 1, 2001

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
10/01/01